

October 29, 2010

## Press Release

Abbott Japan Co., Ltd.  
Eisai Co., Ltd.

### **Abbott Japan and Eisai Receive Approval for Additional Indications of Humira<sup>®</sup>, a Fully Human Anti-TNF $\alpha$ Monoclonal Antibody, for the Treatment of Crohn's Disease and Ankylosing Spondylitis**

Abbott Japan Co., Ltd. (Pharmaceutical Products Group Headquarters: Tokyo, President & CEO: Gary M. Winer, "Abbott Japan") and Eisai Co., Ltd. (Headquarters: Tokyo, President & CEO: Haruo Naito, "Eisai") announced today that they have received approval from the Japanese Ministry of Health, Labour, and Welfare for Crohn's disease and ankylosing spondylitis as additional indications and dosage and administration for Humira<sup>®</sup> pre-filled syringe 40 mg/0.8 mL for subcutaneous injection (generic name: adalimumab [genetical recombination]), a fully human anti-TNF $\alpha$  monoclonal antibody jointly developed by the two companies in Japan. Humira<sup>®</sup> is already indicated in Japan for rheumatoid arthritis (approved in April 2008), plaque psoriasis, and psoriatic arthritis (approved in January 2010).

Humira<sup>®</sup> is a fully human anti-TNF $\alpha$  monoclonal antibody that exerts its effects by neutralizing TNF $\alpha$ , a cytokine that plays a central role in inflammatory responses. While Abbott Japan is the marketing and manufacturing authorization holder of Humira<sup>®</sup> in Japan and Eisai is responsible for its distribution, the two companies are working together to promote the drug.

Crohn's disease is an inflammatory bowel disease characterized by recurrent ulcers and inflammation in the gastrointestinal tract, and the number of patients with it is increasing year on year. In two placebo-controlled, double-blind comparative studies conducted in Japan in patients with moderate or severe Crohn's disease, Humira<sup>®</sup> demonstrated excellent efficacy in inducing and maintaining remission and tolerability equivalent to that observed in foreign studies.

Ankylosing spondylitis is characterized by joint pain and stiffness in the neck, lower back, and hips, and in some cases the hands and feet, which leads to fusion and rigidity of affected joints over time. There was no specific treatment for this chronic systemic inflammatory disease until progress was made in the research and development of anti-TNF $\alpha$  therapies. In clinical studies of Humira<sup>®</sup> conducted in Japan in patients with active ankylosing spondylitis, Humira<sup>®</sup> demonstrated excellent efficacy in improving the signs/symptoms of ankylosing spondylitis and tolerability equivalent to that observed in foreign studies.

By providing Humira<sup>®</sup> as a new treatment option for Crohn's disease and ankylosing spondylitis, Abbott and Eisai will contribute to improving the quality of life (QOL) of patients.

**[Please refer to the following notes for a product outline, a glossary of terms and information on Eisai and Abbott's commitment to immunology]**

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## < Notes to editors >

### 1. About Humira® pre-filled syringe 40 mg/0.8 mL for subcutaneous injection (Underlined information indicates newly approved indications/dosage and administration)

#### 1) Indications

Humira® is indicated for:

Treatment of the following diseases in patients who have had an inadequate response to conventional therapy:

Rheumatoid arthritis

Plaque psoriasis, psoriatic arthritis

#### Ankylosing spondylitis

Induction and maintenance of clinical remission in patients with moderately to severely active Crohn's disease (only in patients who have had an inadequate response to conventional therapy)

#### 2) Dosage and Administration

##### **Rheumatoid Arthritis**

The recommended dose of adalimumab (genetical recombination) in adult patients with rheumatoid arthritis is 40 mg administered subcutaneously every other week. The dose may be increased up to 80 mg when effects are insufficient.

##### **Plaque psoriasis and psoriatic arthritis**

The recommended dose of adalimumab (genetical recombination) in adult patients with plaque psoriasis or psoriatic arthritis is an initial dose of 80 mg administered subcutaneously, followed by 40 mg every other week. The dose may be increased up to 80 mg when effects are insufficient.

##### **Ankylosing spondylitis**

The recommended dose of adalimumab (genetical recombination) in adult patients with Ankylosing spondylitis is 40 mg administered subcutaneously every other week. The dose may be increased up to 80 mg when effects are insufficient.

##### **Crohn's disease**

The recommended dose of adalimumab (genetical recombination) in adult patients with Crohn's disease is an initial dose of 160 mg administered subcutaneously, followed by 80 mg two weeks later. Beginning four weeks after the initial dose, a dose of 40 mg is administered subcutaneously every other week.

## 2. Glossary of Terms

### 1) Crohn's disease

Crohn's disease is a chronic autoimmune disease of unknown etiology that is characterized by ulceration and inflammatory lesions most commonly in the small and large intestines. This inflammation is often accompanied by diarrhea and abdominal pain. The Japanese Ministry of Health, Labour, and Welfare has designated Crohn's disease as a "Specified Disease," a rare and intractable disease for which financial support is provided to those patients afflicted with it. Crohn's disease has become increasingly common over the last 10 years. As of the end of 2008, approximately 29,000 patients were registered as having the disease (data from the Japan Intractable Disease Information Center).

Crohn's disease is more prevalent among males, with a male/female ratio of 2:1, and a peak age of onset of late teens to early twenties. Crohn's disease is characterized by intestinal stenosis, ileus, intestinal abscesses (collections of pus resulting from infection) and perianal fistulas (ulcers in the intestine that form tunnels to surrounding intestinal wall or skin). When signs and symptoms cannot be controlled with nutrition or drug therapy, patients may require surgical treatment. Since patients with Crohn's disease often experience periods of both flare-ups and remission, long-term treatment is required to prevent recrudescence (recurrence of gastrointestinal inflammation) and recurrence (occurrence of inflammation in a new region) even after achieving remission.

## **2) Ankylosing spondylitis**

Ankylosing spondylitis (AS) is a chronic systemic inflammatory disease that manifests first as joint pain and stiffness in the neck, lower back, and hips, and in some cases the hands and feet, followed by fusion and rigidity of affected joints over time. In rare cases, patients may develop severe AS with bony ankylosis or deformation of the spine and other joints. AS typically develops in young individuals, most often men, in their teens and twenties, and progresses slowly over several decades. Although the cause of AS is unknown, it is believed that genetic factors play an important role in the etiology of the disease. The prevalence of AS differs among ethnic groups, and is lower in Japanese (0.0065%) than Caucasians (0.9%).

The most commonly observed initial signs/symptoms of AS are inflammation of ligaments and tendons at their attachments to bone. Affected joints mainly include those of the spine, back joints, sacroiliac joints, and joints between the trunk and the extremities such as shoulder joints and hip joints. Inflammation of affected ligaments and tendons leads to severe degeneration of tissues. Regeneration of degenerated tissue to normal tissue does not occur, and instead calcification or ossification develops, eventually causing fusion of joint bone tissues and resulting in complete rigidity of the joints (on X-ray, rigid spine in AS is termed "bamboo spine"). It sometimes causes systemic symptoms such as mild fever, general malaise and weight loss in addition to pain, limitation of motility, oppressive pain and exercise pain. Patients with AS may also experience various complications such as uveitis, a disorder of the eye.

As for the treatment of AS, it is believed that neutralization of  $TNF\alpha$  may alleviate inflammation of affected joints, since concentration of  $TNF\alpha$ , an inflammatory cytokine, is found at high levels in affected areas such as the sacroiliac joint.

## **3) $TNF\alpha$**

The tumor necrosis factors (TNFs) are a group of cytokines (i.e., substances mediating cell-cell interactions) mediating intercellular communication that have been found to damage tumor cells.  $TNF\alpha$  is produced by many types of cells, including macrophages, lymphocytes, and vascular endothelial cells, and is known to cause and enhance inflammatory responses and to activate inflammatory cells.

## **4) Monoclonal antibody**

A monoclonal antibody is a protein produced from clones of a single antibody-producing cell (called a monoclonal). Using the monoclonal antibody technique, manufacturers can obtain a homologous population of antibody molecules identical in affinity and specificity for the target antigen.

## **3. About Humira®**

Humira® resembles antibodies normally found in the body. It works by blocking tumor necrosis factor alpha ( $TNF\alpha$ ), a cytokine that, when produced in excess, plays a central role in the inflammatory responses of many immune-mediated diseases.

As of June 2010, Humira® has been approved for the treatment of rheumatoid arthritis in 79 countries, psoriatic arthritis in 79 countries, ankylosing spondylitis in 76 countries, Crohn's disease in 75 countries, plaque psoriasis in 75 countries, and juvenile idiopathic arthritis in 50 countries, and more than 460,000 people worldwide have been treated with it.

Humira® has been extensively investigated in a wide range of clinical studies, and a large-scale safety information database has been established containing data on approximately 24,000 patients who received adalimumab for a variety of indications between April 1, 1997 and November 6, 2009. A number of clinical trials are also underway to evaluate the potential of Humira® in treating immune-mediated diseases other than those for which it is currently indicated.

#### **4. Eisai's Commitment to Immunology**

Eisai, whose strength lies in low-molecular-weight drugs, is aggressively addressing the development of biologics. Having acquired Morphotek, Inc., a U.S. bio-venture specialized in the research and development of antibody drugs, in April 2007, Eisai is now involved in the creation of antibody drugs for the treatment of cancer, rheumatoid arthritis, and infectious diseases using Morphotek's proprietary technologies, such as Human Morphodoma® and Libradoma™. In addition, Eisai is working with Sweden-based BioArctic Neuroscience Inc. to investigate potential immunotherapies for Alzheimer's disease, and is developing and marketing Humira®, a fully human anti-TNF $\alpha$  monoclonal antibody, in Japan in cooperation with Abbott Japan, thus demonstrating its commitment to improving the quality of life (QOL) of patients and their families by producing antibody drugs.

#### **5. About Abbott**

Headquartered in Chicago, Illinois, Abbott is a global, broad-based health care company devoted to the discovery, development, manufacture and marketing of pharmaceuticals and medical products, including nutritionals, devices and diagnostics. The company employs nearly 90,000 people and markets its products in more than 130 countries.

In Japan, approximately 2,500 Abbott employees are devoted to the manufacture, development, distribution, and marketing of pharmaceuticals and medical products, including nutritionals, devices, diagnostics, and products for vision care. Abbott's main offices in Japan are located in Tokyo, Fukui, and Chiba. News releases issued by Abbott Japan and Abbott Headquarters are available at [www.abbott.co.jp](http://www.abbott.co.jp) and [www.abbott.com](http://www.abbott.com), respectively.

#### **6. Abbott's Commitment to Immunology**

Abbott is focused on the discovery and development of innovative treatments for immunologic diseases. The Abbott Bioresearch Center, founded in 1989 in Worcester, Mass., United States, is a world-class discovery and basic research facility committed to finding new treatments for autoimmune diseases.

More information about Humira®, including full prescribing information, is available on the Web sites <http://www.e-humira.jp> (Japanese only) and [www.HUMIRA.com](http://www.HUMIRA.com) (English).